REMARKS

Upon entry of these amendments, claims 1-7 and 24-31 are pending. Claims 1, 4, and 6 have been amended and new claims 24-31 have been added. Support for these amendments can be found throughout the specification and original claims as filed. The specification has been amended to insert SEQ ID NOs and to insert the enclosed sequence listing in accordance with 37 C.F.R. §§ 1.831-1.825. No new matter has been added.

The Sequence Listing

The Examiner has indicated that the application does not comply with the sequence listing requirements of 37 C.F.R. §§ 1.831-1.825. Applicants have filed herewith a sequence listing in paper form, a CRF, and a Statement in Support of CRF. Thus, this objection has been overcome and can be withdrawn.

Claim Rejections -- 35 U.S.C. § 102(a)

Bhattacharya

Claims 1-2 and 4-5 have been rejected under 35 U.S.C. § 102(a) as anticipated by Bhattacharya et al., Genes and Development 13:64-75 (1999) ("Bhattacharya"). The Examiner states that Bhattacharya "recites a method for identifying a compound that modulates a transcriptional response to hypoxia in a cultured cell." (Office action, page 4). Independent claim 1 has been amended herein to require that the claimed method be practiced "*in vivo*." Dependent claims 2, 4-5, and newly added claims 24-25, depend directly or indirectly from claim 1 and thus contain all the limitations of amended claim 1. The Examiner states that the prior art does not teach or render obvious a method for identifying compounds that modulate a transcriptional response to hypoxia wherein the method takes place *in vivo*. (Office action, page 8). Therefore, Applicants assert that claims 1-2 and 4-5, as amended herein, and new claims 24-25 are not anticipated by Bhattacharya.

The Examiner has also rejected claims 3 and 7 under 35 U.S.C. § 102(b) as anticipated by Bhattacharya. Claims 3 and 7 depend directly or indirectly from claim 1 and thus contain all the limitations of amended claim 1. Since amended claim 1 has been demonstrated above to be not anticipated by Bhattacharya, claims 3 and 7 are also not anticipated by this reference.

New independent claim 26, and dependent claims 27-31, are drawn to *in vitro* methods of

identifying a compound that modulates a transcriptional response to hypoxia in a cell and recite, in part, the steps of "providing a candidate compound [...and] contacting said candidate compound with a cell or the extracellular environment of a cell containing a hypoxia-responsive promoter or an endogenous hypoxia-responsive gene." In contrast, Applicants assert that Bhattacharya does not teach or suggest the provision of a candidate compound to the cell or the extracellular environment of the cell. Rather, Bhattacharya teaches the endogenous production of p35srj polypeptides generated inside the cell either by the endogenous p35srj gene or transfected p35srj expression vectors. (See, Bhattacharya, Figures 2D and 5C). Thus, since Bhattacharya does not disclose the "providing" of an exogenous compound to the cell or extracellular environment of a cell as recited in new claims 26-31, this reference cannot anticipate these claims.

Ebert

Claims 1-2 and 4-5 have been rejected under 35 U.S.C. § 102(a) as anticipated by Ebert et al., Mol. Cell Biol. 18:4089-96 (1998) ("Ebert"). The Examiner states that Ebert "recites a method for identifying a compound that modulates a transcriptional response to hypoxia in a cultured cell (i.e. Hepa-1 cells)." (Office action, page 4). As stated above in regard to Bhattacharya, amended claims 1-2 and 4-5 require that the claimed method be practiced "*in vivo*." The Examiner states that the prior art does not teach or render obvious a method for identifying compounds that modulate a transcriptional response to hypoxia wherein the method takes place *in vivo*. (Office action, page 8). Therefore, Applicants assert that claims 1-2 and 4-5, as amended herein, and new claims 24-25 are not anticipated by Ebert.

Applicants assert that new independent claim 26, and dependent claims 27-31, drawn to *in vitro* methods of identifying a compound that modulates a transcriptional response to hypoxia are not anticipated by Ebert for the reasons discussed above in regard to Bhattacharya. Specifically, Ebert teaches the endogenous production of PK-A and CREB polypeptides generated inside the cell by transfected expression vectors. (See, Ebert, Figures 4A and 5). Thus, Ebert, like Bhattacharya, is fatally deficient in that Ebert does not disclose the "providing" of an exogenous compound to the cell or extracellular environment of a cell as recited in new claims 26-31, this reference cannot anticipate these claims.

For the above-stated reasons, Applicants request that this rejection be withdrawn.

Claim Rejections -- 35 U.S.C. § 102(b)

Arany

Claims 1-5 have been rejected under 35 U.S.C. § 102(b) as anticipated by Arany et al., PNAS 93:12969-12973 (1996) ("Arany"). The Examiner states that Arany "recites a method for identifying a compound that modulates a transcriptional response to hypoxia in a cultured cell (Hep3B cells)." (Office action, page 6). As stated above in regard to Bhattacharya and Ebert, amended claims 1-5 require that the claimed method be practiced "*in vivo*." The Examiner states that the prior art does not teach or render obvious a method for identifying compounds that modulate a transcriptional response to hypoxia wherein the method takes place *in vivo*. (Office action, page 8). Therefore, Applicants assert that claims 1-5, as amended herein, and new claims 24-25 are not anticipated by Arany.

Applicants assert that new independent claim 26, and dependent claims 27-31, drawn to *in vitro* methods of identifying a compound that modulates a transcriptional response to hypoxia are not anticipated by Arany for the reasons discussed above in regard to Bhattacharya and Ebert. Specifically, Arany teaches the endogenous production of p300/CREB polypeptides generated inside the cell by transfected expression vectors. (See, Arany, page 12969 and Figures 1A-B). Thus, Arany, like Bhattacharya and Ebert, is fatally deficient in that Arany does not disclose the "providing" of an exogenous compound to the cell or extracellular environment of a cell as recited in new claims 26-31, this reference cannot anticipate these claims.

Fandrey

Claims 1, 2, 4 and 5 have been rejected under 35 U.S.C. § 102(b) as anticipated by Fandrey et al., Biochem. J. 303:507-10 (1994) ("Fandrey"). The Examiner states that Fandrey "recites a method for identifying a compound that modulates a transcriptional response to hypoxia in a cell (cultured cell line HepG2)." (Office action, page 6). As stated above in regard to Bhattacharya, Ebert, and Arany amended claims 1, 2, 4 and 5 require that the claimed method be practiced "*in vivo*." The Examiner states that the prior art does not teach or render obvious a method for identifying compounds that modulate a transcriptional response to hypoxia wherein the method takes place *in vivo*. (Office action, page 8). Therefore, Applicants assert that claims 1, 2, 4 and 5, as amended herein, and new claims 24-25 are not anticipated by Fandrey.

Applicants assert that new independent claim 26, and dependent claims 27-31, drawn to *in vitro* methods of identifying a compound that modulates a transcriptional response to hypoxia are not anticipated by Fandrey for the reasons discussed above in regard to Bhattacharya, Ebert, and Arany. Specifically, Fandrey teaches the endogenous production of erythropoietin induced by hydrogen peroxide; the erythropoietin is generated inside the cell. (See, Fandrey, page 507 and Figures 2A-B). Thus, Fandrey, like Bhattacharya, Ebert, and Arany is fatally deficient in that Fandrey does not disclose the "providing" of an exogenous compound to the cell or extracellular environment of a cell as recited in new claims 26-31, this reference cannot anticipate these claims.

Claim Rejections -- 35 U.S.C. § 112, 2nd Paragraph

Claims 1-7 have been rejected under 35 U.S.C. § 112, 2nd paragraph, as indefinite. The Examiner states that claim 1 is indefinite in the absence of a comparison to a control of some kind. (Office action, page 7). Applicants note that claim 1 has been amended herein to recite the phrase "wherein an increase or decrease in the transcriptional response to hypoxia in the cell in the presence of the candidate compound compared to the transcriptional response to hypoxia in a cell in the absence of the candidate compound indicates that the candidate compound modulates the transcriptional response to hypoxia." Thus, Applicants have provided the comparison requested by the Examiner in the Office action, and assert that this rejection has been overcome and can be withdrawn.

The Examiner also states that Claim 4 is vague in the recitation of the term "ortransferrin," and that the abbreviated terms "iNOS" and "ALDA" have not been spelled out. Applicants have amended claim 4 herein to correct this typographical error by inserting a space after the word "or," and have spelled out the complete names of inducible nitric oxide synthase and aldolase A. These rejections have been overcome and can be withdrawn.

CONCLUSION

Based on the instant amendments and remarks, Applicants submit that this application is in condition for allowance and such action is respectfully requested. Should any questions or issues arise concerning the application, the Examiner is encouraged to contact Applicants' undersigned attorney at the telephone number indicated below.

Respectfully submitted,

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